

**REMARKS**

Claims 1, 2, 10-14 and 28-82 are all the claims pending in the application.

After entry of this Amendment, claims 1, 2 and 10-14 will be canceled and claims 28-82 will be pending.

The claims have been amended to make the use of plural forms of words consistent.

No new matter has been added. Entry of the Amendment is respectfully requested

**I. Formal Matters**

**A.** Applicant thanks the Examiner for the helpful interview held in her office on June 4, 2004. In view of the points discussed during the interview, Applicant now presents this instant Amendment and Request for Reconsideration.

**B.** Applicant notes that an Information Disclosure Statement and reference list was filed in this application on October 29, 2003. As it was not included with the Advisory Action dated April 15, 2004, Applicant respectfully requests the Examiner to provide Applicant with a copy of the initialed and signed reference list. Applicant includes a copy of the reference list herewith for the Examiner's convenience.

**C.** Applicant renews his request for acknowledgement of Applicant's claim for domestic priority to U.S. provisional application number 60/268,326, filed February 14, 2001. Applicant respectfully requests such acknowledgement be made in the next paper issued by the U.S. PTO.

**II. Rejection of Claims Under 35 U.S.C. §112**

**A.** At paragraph 5 of the Office Action dated December 10, 2004, claims 1, 2 and 10-14 were rejected under 35 U.S.C. §112, first paragraph, as lacking adequate written description support.

In the Advisory Action dated April 15, 2004, the Examiner notes that based on the Response filed by Applicant on March 20, 2004, the rejection of claims 1, 2 and 10-14 under 35 U.S.C. §112, first paragraph, has been withdrawn.

**B.** At paragraph 4 of the Office Action dated December 10, 2004, claims 28-45 and 67-82 were rejected under 35 U.S.C. §112, first paragraph, as lacking adequate written description support.

The Examiner stated that the claims were rejected in view of the recitation of the negative limitation “an extrinsic fluorescent marker is not part of the system.” The Examiner explained that negative limitations must have support in the original disclosure and that the mere absence of a positive recitation is not a basis for exclusion.

In the Response filed March 10, 2004, Applicant pointed to the location of support for the recitation of the negative limitation in the specification.

In the Advisory Action dated April 15, 2004, the Examiner maintained the rejection and stated that the statement in the specification that “such extrinsic fluorophores can be covalently or non-covalently attached to the biomolecule” (page 4, lines 3-4) indicates that the extrinsic fluorophore is part of the system.

During the interview held with the Examiner on June 4, 2004, it was explained to the Examiner (and support was presented as discussed below) that the present invention

encompasses two types of systems, those that rely on intrinsic fluorescence alone, and those that additionally use an extrinsic fluorescent marker. The sentence noted by the Examiner above refers to those systems that additionally use an extrinsic fluorescent marker. It merely notes that in such systems, the extrinsic marker may be attached to the biomolecule in one of two manners, covalently or non-covalently.

During the interview, the Examiner's attention was directed to specific passages of the specification that describe the systems claimed in the instant application as including both those systems that rely on intrinsic fluorescence alone, and those systems that additionally use an extrinsic fluorescent marker. In particular, the Examiner's attention was drawn to page 16, paragraph 76, of the specification where it is stated that "the present invention discloses a novel method for the detection of nucleic acid sequences by increasing the intrinsic fluorescence of the nucleic acids." As further stated in the same paragraph, "**the present invention does not require the use of an extrinsic probe.**"

The Examiner's attention was also drawn to paragraph 77, lines 19-21, where it is stated that "the identification of nucleic acids using the intrinsic fluorescence of the nucleic acid **eliminates the requirement for extrinsic probes.**"

The Examiner agreed during the interview that based on these passages, there is support for the negative claim limitation in the specification.

Applicant also refers back to the Response Under 37 C.F.R. §1.116 filed March 10, 2004, for the location of further support for the negative limitation.

Thus, Applicant respectfully asserts that "alternative elements are positively recited" in the specification, as contemplated by MPEP §2173.05(i), where it is stated that "if alternative

elements are positively recited in the specification, they may be explicitly excluded in the claims.”

Applicants therefore respectfully traverse the Examiner’s position that the claims reciting negative limitations do not have support in the original disclosure, and requests reconsideration and withdrawal of this rejection.

### **III. Rejection of Claims Under 35 U.S.C. §102**

At paragraph 7 of the Office Action dated December 10, 2004, claims 1-2 and 10-14 were rejected under 35 U.S.C. §102(b) as being anticipated by Schalkhammer et al. (USSN 5,866,433).

Applicant includes herewith an amendment canceling the rejected claims (without prejudice to filing the canceled claims in a continuing application), thus rendering this rejection moot.

### **IV. Rejection of Claims Under 35 U.S.C. §103**

At paragraph 9 of the Office Action dated December 10, 2004, claims 46-66 were rejected under 35 U.S.C. §103(a) as being obvious over Schalkhammer et al. in view of Natan et al. (USSN 6,149,868).

The Examiner stated that while Schalkhammer et al. does not teach a system comprising a colloidal suspension of one or more metal particles, Natan et al. provides the missing element. The Examiner concluded that it would have been obvious to combine and substitute a system comprising a colloidal suspension of one or more metal particles of Natan et al. in the system of Schalkhammer et al., because Natan et al. states “in yet another embodiment, detection is accomplished at extremely low analyte concentrations.” The Examiner explained that the

ordinary practitioner would have been motivated to combine and substitute a system comprising a colloidal suspension in the system of Schalkhammer et al. to improve concentration determination and provide a system wherein detection is accomplished at extremely low analyte concentrations.

In the Response filed March 10, 2004, Applicant discussed differences between the combination of Schalkhammer et al. and Natan et al., and provided reasons why the combination did not render the present invention obvious.

In the Advisory Action dated April 15, 2004, the Examiner stated that the limitations allegedly argued by Applicant were not commensurate with the actual claim language.

During the interview held with the Examiner on June 4, 2004, two primary reasons why the combination of Schalkhammer et al. and Natan et al. does not render the invention claimed in the rejected claims obvious were discussed with the Examiner.

The first reason was based on the difference in what is being detected by the invention of Natan et al. and what is being detected in the system recited in Applicant's claims. It was noted that Natan et al. discloses a nanometer-scale structure from which surface enhanced Raman scattering (SERS) measurements can be taken. SERS measurements are based on vibrational spectral intensities of the biomolecule in the analyte. Thus, the structure of Natan et al. provides an enhancement in vibrational spectral intensities and it is the **vibrational spectral intensities** that are detected in the system of Natan et al. (col. 1, lines 16-20; col. 5, lines 40-56).

In contrast, the system of the pending claims and Schalkhammer et al. is based on the measurement of fluorescent intensity. The skilled artisan seeking to improve the system of Schalkhammer et al. would not have been motivated to use a suspension of metal particles as

taught by Natan et al., in the system of Schalkhammer et al., because there was (1) no motivation to combine the references and (2) no expectation of success, given that the teachings of Natan et al. are limited to increasing vibrational spectral intensities and disclose nothing with regard to fluorescent intensities.

The second reason discussed with the Examiner as to why the combination of Schalkhammer et al. and Natan et al. does not render the invention recited in the rejected claims obvious was based on the physical differences in the structure of Natan et al., and that of the pending application.

Natan et al. teaches the use of a sandwich of an analyte (such as a protein) between a colloidal metal nanoparticle and a SERS substrate (e.g., a macroscopic silver particle). Thus, the structure in Natan et al. is a combination of **three different categories of components**, (1) nanometer-sized metal particles, (2) biomolecules and (3) SERS substrates. It is the sandwich of these three elements that is the basis of the invention. The improvements over the art are discussed in col. 2, lines 49-62. Use of this structure allows for “exceedingly low” amounts of an analyte (see, e.g., col. 3, lines 5-8). Each description of the structure of Natan et al. states that it is a “deliberately-prepared sandwich structure” (see, e.g., col. 3, lines 2, 6 and 11; claim 1). None of the embodiments of Natan et al. appear to use less than these three components.

In contrast, the system recited in the rejected claims comprises metal particles and biomolecules. Thus, there are only **two different categories of components** required for use in the system of the rejected claims, (1) metal particles and (2) biomolecules. Therefore, even if the disclosure of Natan et al. was combined with the teachings of Schalkhammer et al., the skilled artisan would not arrive at the invention of the rejected claims.

The Examiner agreed during the interview that based on these two differences, the invention recited in the rejected claims is not rendered obvious by the combination of Schalkhammer et al. and Natan et al.

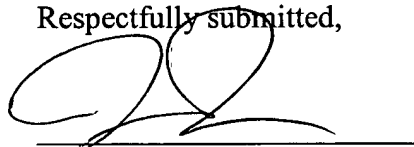
For these reasons, and those further discussed in the Response filed March 10, 2004, Applicant respectfully requests reconsideration and withdrawal of this rejection.

**V. Conclusion**

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



Drew Hissong  
Registration No. 44,765

SUGHRUE MION, PLLC  
Telephone: (202) 293-7060  
Facsimile: (202) 293-7860

WASHINGTON OFFICE

**23373**

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